UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF PREVENTION,
PESTICIDES AND TOXIC SUBSTANCES

EPA File Symbol 66222-LT 57

23/DEC/2002

MEMORANDUM

Subject: EPA I.D. No: 2F06430 RimOn 7.5 WDG
DP Barcode: D285480
Case No: 295018
PC Code: 124002

From: Masih Hashim, Toxicologist MH
Technical Review Branch SCR
Registration Division (7505C)

To: Suku Oonnithan, PM Team 04
Insecticide-Rodenticide Branch
Registration Division (7505C)

Applicant: Makhteshim-Agan of North America
551 Fifth Avenue
New York, NY 10176

FORMULATION FROM LABEL:

Active Ingredient(s):	% by wt.
Novaluron	7.5
Inert Ingredients/related deravatives	92.5
Total:	100.0

ACTION REQUIRED: PM requests a review of the acute toxicity data for the Rimon 7.5 WDG, 2F06430.

BACKGROUND: Makhteshim-Agan of North America has submitted a set of toxicity studies to support the registration of its Product Rimon 7.5 WDG. The animal studies were conducted at the Huntingdon Research Centre and Safepharm Laboratories in UK.

RECOMMENDATIONS: Each of the following studies (MRID 456384-21 through 25) is in compliance with the Sub Division F guidelines.

TRB can use the cited inhalation study as requested by the Registrant (2-20-02).

The Company's label is consistent with the toxicology profile of the product:

acute oral toxicity	IV	acceptable	MRID 456384-21
acute dermal toxicity	IV	acceptable	MRID 456384-22
acute inhalation	IV	cited	MRID 452035-05
primary eye irritation	II	acceptable	MRID 456384-23
primary dermal irritation	III	acceptable	MRID 456384-24
dermal sensitization	neg.	acceptable	MRID 456384-25

LABELING:

PRODUCT ID #: 2F06430

Product Name RimOn 7.5 WDG
PRECAUTIONARY STATEMENTS
SIGNAL WORD: WARNING

Hazards to Humans and Domestic Animals:

Causes substantial but temporary eye injury. Harmful if absorbed through skin. Harmful if swallowed. Do not get in eyes or on clothing. Wear protective eye wear (goggles, face shield, or safety glasses). Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, or using tobacco. Remove and wash contaminated clothing before reuse.
Avoid contact with skin, eyes or clothing. Wear long-sleeved shirt and long pants, socks, shoes, and gloves. ~~Wear: Long-sleeved shirt and long pants, Socks, Shoes, and gloves.~~

First Aid:

If in eyes:
-Hold eye open and rinse slowly and gently with water for 15-20 minutes.
-Remove contact lenses, if present, after the first 5 minutes, then continue rinsing.
-Call a poison control center or doctor for treatment advice.

If on skin:
-Take off contaminated clothing.
-Rinse skin immediately with plenty of water for 15-20 minutes.
-Call a poison control center or doctor for treatment advice.

NOTE TO PHYSICIAN: Note to PM/CRM/Registrant: The proposed label should contain a "Note to Physician". The following statements are suggested types of information that may be included, if applicable: - technical information on symptomatology; - use of supportive treatments to maintain life functions; - medicine that will counteract the specific physiological effects of the pesticide; - company telephone number to specific medical personnel who can provide specialized medical advice.

Have the product container or label with you when calling a poison control center or doctor or going for treatment.

DATA EVALUATION RECORD

STUDY TYPE: ACUTE ORAL TOXICITY TESTING (870-1100)

PRODUCT MANAGER: 04 **REVIEWER**: M. HASHIM

TEST MATERIAL: "RIMON" 7.5WDG, Novaluron (7.9%) active ingredient. Brown granules Batch No. 001113

CITATION: Blanchard, E. L. (2001) Rimon 7.5 WDG: Acute Oral Toxicity Study in the Rat. Huntingdon Life Sciences, Cambridgeshire, England. Study No. MAK 685/012647/AC date 5-24- 01. MRID 456384-21. Unpublished.

SPONSOR: Makhteshim-Agan of North America, New York, NY 10176

EXECUTIVE SUMMARY: In an acute oral toxicity study (MRID 456384-21), "RIMON" 7.5WDG (Novaluron 7.9%) was administered to 3 male and 3 female SD rats (Hsd Av. Wt. 207-240 g, Harlan U.K. Bicester, Oxon, England) as a single dose by gavage (formulated in 1% w/v methylcellulose) at 5000 mg/kg body weight. In life parameters included signs of gross toxicity and mortality for a subsequent period of 14 days. Initial and weekly body weights and terminal necropsy findings were recorded.

Oral LD_{50} for "RIMON" 7.5WDG in male/ female rats was determined to be > 5000 mg/kg. The study is classified as Tox Category IV.

There were no deaths on the study. Clinical signs in the treated animals were piloerection, hunched posture, lethargy and abnormal gait. There was increased salivation, partially closed eyelids, noisy and shallow respiration, reduced body temperature, prostration, dull eyes, reduced body tone, loose feces, pallor of the skin, abnormal colored urine, staining around muzzle, thin appearance, body tremors and lacrimation. Only one animal lost body weight on days 8 and 15. Necropsy findings were not significant.

This study (870-1100) is Acceptable in accordance with the Sub-Division F guideline.

COMPLIANCE: The study is in compliance with GLP, signed and dated. .

RESULTS:

Number of Deaths/ Number tested

Dosage mg/kg	Male	Female	Total
5000	0/3	0/3	0/6

Necropsy Findings: Unremarkable.

DATA EVALUATION RECORD

STUDY TYPE: ACUTE DERMAL TOXICITY TESTING (870-1200)

PRODUCT MANAGER: 04 **REVIEWER**: M. HASHIM

TEST MATERIAL: "RIMON" 7.5WDG, Novaluron (7.9%) active ingredient. Brown granules Batch No. 001113

CITATION: Blanchard, E. L. (2001) Rimon 7.5 WDG: Acute Dermal Toxicity to the Rat. Huntingdon Life Sciences, Cambridgeshire, England. Study No.MAK 685/012647/AC date 5-24-01. MRID 456384-22. Unpublished.

SPONSOR: Makhteshim-Agan of North America, New York, NY 10176

EXECUTIVE SUMMARY: In an acute dermal toxicity study (MRID 456384-22) with "RIMON" 7.5WDG , (Novaluron 7.9%), 5 male and 5 female SD rats (Hsd Av. Wt. 211-250 g, Harlan U.K. Bicester, Oxon, England) were topically applied with a single dose at 5000 mg/kg body weight. The test substance was formulated at a maximum (practical) concentration in a 1% w/v aqueous methylcellulose at a dose volume of 6.0 ml/kg and applied over the (prepared) skin (50x50 mm dorso lumbar region). This was covered by a porous gauze held in place with a dressing. The wrappings were removed after 24 hours and the test sites were washed/cleaned then evaluated. Animals were observed for mortality and signs of gross toxicity for 14 days. Weekly body weights and terminal necropsy findings were recorded on all animals.

Dermal LD_{50} for "RIMON" 7.5WDG was > 5000 mg/kg in male/female rabbits. The test substance is classified as tox Category IV.

There was no lethality or compound related toxic signs. There was no adverse effect on the body weight gains. There was local dermal effect such as: very slight to slight dermal irritation (Grade 1 erythema with or without Grade 1 or 2 edema) as noted in 7 of 10 animals following removal of dressing. This lesion resolved by Day 11. Scabs/scabbing was also observed in 2 of 10 animals in the later part of the study. Three of 10 animals showed no dermal response. There were no (other) significant necropsy findings.

This study (870-1200) is Acceptable in accordance with the Sub-Division F guideline.

COMPLIANCE: The study is in compliance with GLP, signed and dated.

RESULTS:
Number of Deaths/ Number tested

Dosage mg/kg	**Male**	**Female**	**Total**
5000	0/5	0/5	0/10

OBSERVATIONS: There was no lethality or compound related toxic signs. Local dermal effects are described above. There was no effect on the body weight gains.

NECROPSY FINDINGS: Local dermal effects as described above.

DATA EVALUATION RECORD

STUDY TYPE: PRIMARY EYE IRRITATION TESTING (870-2400)

PRODUCT MANAGER: 04 **REVIEWER**: M. HASHIM

TEST MATERIAL: "RIMON" 7.5WDG, Novaluron (7.9%) active ingredient. Brown granular solid, Batch No. R-903

CITATION: Dreher, D. M. (2000) Rimon 7.5 WDG: Acute Eye Irritation in the Rabbit. Safepharm Laboratories, Derby, UK. Project No. 306/362/ dated 9-19-00. MRID 456384-24. Unpublished.

SPONSOR: Makhteshim-Agan of North America, New York, NY 10176

EXECUTIVE SUMMARY: In a primary eye irritation study (MRID 456384-24), 88 mg (0.1 ml equivalent) of "RIMON" 7.5WDG (Novaluron 7.9%) was placed into the conjunctival sac of the right eye of 3 NZW rabbit (Source: David Percival, Moston, Sandbach, Cheshire, UK). The eye lid of the first rabbit was held closed for one second after instillation, and the other eye remained untreated and served as the control. The pain was assessed then the other two rabbits were instilled (eye) after treating them with a local anesthetic. The eyes were examined for irritation such as abnormalities of cornea, iris and conjunctiva up to 21 days.

Ocular irritation started as of 1st hour affecting conjunctiva and iris then cornea (Table 1). Maximum group mean score was 48.3. All irritation subsided within 21 days. The product "RIMON" 7.5WDG is a severe irritant.

This study (870-2400) is in compliance with the Sub Division F guidelines. It is classified as Tox Category II.

COMPLIANCE: The study meets GLP requirements.

RESULTS:

Table 1. Number of eye lesions/ Total number of eyes affected

Lesion	1 hr	24	48	72	7 days	14	21
Cornel opacity	1/3	3/3	3/3	3/3	3/3	3/3	0/3
Iritis	3/3	3/3	3/3	3/3	0/3	0/3	0/3
Conjunctivitis	3/3	3/3	3/3	3/3	1/3	0/3	0/3

DATA EVALUATION RECORD

STUDY TYPE: PRIMARY DERMAL IRRITATION TESTING (870-2500)

PRODUCT MANAGER: 04 **REVIEWER**: M. HASHIM

TEST MATERIAL: "RIMON" 7.5WDG, Novaluron (7.9%) active ingredient. Brown granules Batch No. 001113

CITATION: Blanchard, E. L. (2002) Rimon 7.5 WDG: Skin Irritation to the Rabbit. Huntingdon Life Sciences, Cambridgeshire, England. Study No.MAK 687/012731/AC date 5-24-01. MRID 456384-23. Unpublished.

SPONSOR: Makhteshim-Agan of North America, New York, NY 10176

EXECUTIVE SUMMARY: In a primary dermal irritation study (MRID 456384-23), 0.5 ml of "RIMON" 7.5WDG (Novaluron 7.9%) moistened in distilled water, was topically applied to the intact skin (10 cm^2) of 3 NZW rabbits (Source: Ray Nichols Rabbitry, Lumberton, TX). The site was covered with gauze and elastic adhesive dressing. The dressing was removed and skin cleaned/ washed after 4 hours.. Observations for dermal irritation and any other adverse effects were made at timely intervals of 1, and days 2, 3 and 4.

There was slight erythema in 2 of 6 animals which subsided within 72 hours. The Mean Score for these reactions at 25, 49 and 73 hours after administration calculated separately for each animal was '1' for erythema and '0' for edema. The test substance "RIMON" 7.5WDG is considered as a moderate irritant.

The study is classified as Tox Category III.

The study (870-2500) is Acceptable in accordance with the Sub Division F guideline.

COMPLIANCE: The study is in compliance with GLP, singed and dated.

OBSERVATIONS: There was slight erythema in 2 of 6 animals which subsided within 72 ours. The Means of the Scores for these reactions at 25, 49 and 73 hours after administration calculated separately for each animal was '1' for erythema and '0' for edema.

DATA EVALUATION RECORD

STUDY TYPE: DERMAL SENSITIZATION TESTING (870-2600)

PRODUCT MANAGER: 04 **REVIEWER**: M. HASHIM

TEST MATERIAL: "RIMON" 7.5WDG, Novaluron (7.9%) active ingredient. Brown granular solid Batch No. R 903

CITATION: Dreher, D. M. (2000) Rimon 7.5 WDG: Magnusson and Kligman Maximization Skin Sensitization Study in the Guinea Pig. Safepharm Laboratories, Derby, UK. Project No. 306/363 dated 9-19-00. MRID 456384-25. Unpublished.

SPONSOR: Makhteshim-Agan of North America, New York, NY 10176

EXECUTIVE SUMMARY: A Maximization study (MRID 456384-25) was conducted to assess the sensitization potential of "RIMON" 7.5WDG (Novaluron 7.9%) in Dunkin Hartley guinea pigs (Source: David Hall, Burton on Trent, Staffordshire, UK, Wt. 370-449 g). Ten test and 5 control animals were used for the main study. Using the test substance, the following dose preparations were made based on preliminary screening: Intradermal injection 0.5% w/w in distilled water 0.5% w/w in a mixture of Freund's Complete Adjuvant plus distilled water (1:1); topical application 10% w/w in distilled water; and topical challenge with 5% and 2% w/w distilled water.

The test substance "RIMON" 7.5WDG produced no positive reaction in 10 of 10 test animals. The test substance is not considered a dermal sensitizer.

COMPLIANCE: The test (870-2600) meets GLP requirements. It is Acceptable in accordance with the Sub Division F guide line.

ACUTE TOX ONE-LINERS

1. DP BARCODE: D285480
2. PC CODE: 124002
3. CURRENT DATE: 23/DEC/2002
4. TEST MATERIAL: Novaluron 7.5%

Study/Species/Lab Study #/Date	MRID	Results	Tox. Cat.	Core Grade
Acute oral toxicity study /rat/ Huntingdon Life Sciences/ MAK 685/012647/AC/ 5-24-01	456384-21	LD_{50} > 5000 mg/kg	IV	A
Acute dermal toxicity study /rat/ Huntingdon Life Sciences/ MAK 685/012647/AC/ 5-24-01	456384-22	LD_{50} > 5000 mg/kg	IV	A
Primary eye irritation study/ rabbit/ Huntingdon/ SPL 306/362/ 9-19-00	456384-24	severe irritant	II	A
Primary dermal irritation/ rabbit/ Huntingdon Life Sciences/ MAK 687/012731/AC/ 5-24-01	456384-23	moderate irritant	III	A
Skin sensitization /guinea pigs/ Safepharm Labs/ SPL Project No. 306/363/ 9-19-00	456384-25	negative	-	A

Core Grade Key: A =Acceptable, S = Supplementary, U = Unacceptable, V = Self Validated